JACC Vol 2, No 1
July 1983:70–6

METHODS

Quantitative Assessment of Segmental Wall Motion Abnormalities at Rest and After Atrial Pacing Using Digital Intravenous Ventriculography

G. B. JOHN MANCINI, MD, FRCP (C), SHARON L. NORRIS, MD, KIRK L. PETERSON, MD, FACC, GABRIEL GREGORATOS, MD, FACC, THOMAS F. WIDMANN, MD, WILLIAM L. ASHBURN, MD, CHARLES B. HIGGINS, MD, FACC, with the technical assistance of Ellen Einsidler, RT

San Diego, California

Digital intravenous ventriculography lends itself readily to quantitative assessment of ventricular wall motion with computer algorithms. Forty-five patients referred for cardiac catheterization were studied by digital intravenous ventriculography (mask mode) and direct ventriculography in the 30° right anterior oblique position. Quantitative wall motion was analyzed by a radial shortening method applied to both studies. Lower limits of normal radial shortening were determined for each technique and used to determine the presence or absence of wall motion disorders. The inter- and intraobserver variability of radial shortening measurements was ± 5.3 and ± 8.8%, respectively, with maximal discrepancies of −6 and +7% fractional shortening units. The overall agreement between the two techniques in wall motion assessment was 87% (274 of 315 radii). A subset of patients also underwent atrial pacing, and a second digital intravenous ventriculogram was obtained (5 normal subjects and 15 patients with coronary artery disease). Although analysis of wall motion at rest showed a poor sensitivity for detection of significant coronary stenoses, nine of nine patients with coronary artery disease and normal wall motion at rest showed a quantitative decrease in radial wall motion after atrial pacing.

Thus, digital intravenous ventriculograms can be used to provide quantitative wall motion analyses that show a high degree of agreement with those of standard, direct left ventriculography. Atrial pacing can be used to increase the sensitivity of wall motion analysis for the detection of significant coronary disease.

Digital intravenous ventriculography lends itself readily to the quantitative study of left ventricular function. Although this technique has been validated for the quantitation of left ventricular volumes and ejection fraction (1–4), little information is available about its utility in assessing segmental left ventricular function. Quantitation of wall motion by intravenous digital methods is particularly attractive for several reasons: 1) the interobserver variability of qualitative assessment of wall motion is well known (5); 2) quantitative analysis can be tedious when attempted without computer techniques (6–11); 3) the low fluoroscopic radiation exposure levels employed allow for repeated studies in the same patient without an increase in radiation exposure and with the added possibility of assessing ventricular function in response to interventions; and 4) segmental wall motion analysis requires that ectopic rhythm be absent during the phase of left ventricular imaging (12). This is frequently not the case with direct ventriculography, but arrhythmia can be largely obviated with intravenous contrast injections. The importance of establishing the accuracy of segmental wall motion analysis by digital intravenous methods as compared with the usual methods of direct left ventriculography is therefore apparent.

This study was designed to compare the ability to analyze quantitative segmental wall motion from digital intravenous ventriculograms and from direct left ventriculograms by applying a simple radial shortening method to each study. Criteria for designating a deterioration in segmental function in response to ischemia induced by atrial pacing were also established.

From the Departments of Cardiology and Radiology, University Hospital, University of California at San Diego, San Diego, California. Dr. Mancini was supported by the Canadian Heart Foundation, Ottawa, Ontario, Canada. Manuscript received November 9, 1982; revised manuscript received February 8, 1983, accepted February 11, 1983.

Address for reprints: G. B. John Mancini, MD, Division of Cardiology (H-811A), University Hospital, 225 Dickinson Street, San Diego, California 92103.

0735-1097/83/$3.00

Methods

Study patients. All patients referred for the evaluation of a chest pain syndrome were eligible for this study except those with clear evidence of unstable angina, acute or recent myocardial infarction or renal insufficiency. Forty-five patients were studied. On the basis of coronary arteriography, 11 had normal coronary arteries and 34 had significant coronary stenoses (>70%) of at least one major coronary vessel. The normal group included three men and eight women with a mean age of 53 ± 14 years (mean ± 1 standard deviation). The coronary artery disease group consisted of 27 men and 7 women with a mean age of 59 ± 11 years. Sixteen patients in this group had a history of remote infarction as evidenced by typical symptoms, serum enzyme elevations and development of Q waves on the electrocardiogram at rest.

Clinical protocol. All patients underwent cardiac catheterization by the Sones or Judkins technique. In addition, a 7 French National Institutes of Health venous catheter was advanced to a level just cephalad to the right atrium. A 7 French bipolar pacing electrode was advanced, via a second venous puncture, into the right atrial appendage in a subset of 20 patients (5 normal and 15 with coronary disease). In all patients, both a digital intravenous ventriculogram and a direct left ventriculogram were obtained in the 30° right anterior oblique projection during held inspiration. In addition, a second digital intravenous ventriculogram was obtained immediately after rapid atrial pacing in the subset of 20 patients. All studies were performed on the same day during a single complete cardiac catheterization. The digital studies were performed before direct left ventriculography and coronary arteriography. Sodium meglumine diatrizoate (Renografin-76) was administered by power injection in all studies (36 to 49 cc over 3.0 to 3.5 seconds for the direct left ventriculogram; 40 cc over 2 seconds for the intravenous ventriculogram), and each ventriculogram was performed 15 to 20 minutes apart.

Rapid atrial pacing was performed in 20 patients in a stepwise fashion until the onset of chest pain or a maximal rate of 160 beats/min was reached (13). Two patients were given atropine, 0.6 mg intravenously, to overcome Wenckebach conduction at atrial pacing rates of less than 120 beats/min and before the onset of limiting symptoms. Initially, all studies were obtained at a control heart rate and then at the intrinsic heart rate after cessation of rapid atrial pacing. Subsequently, to ensure greater uniformity of the control and postpacing heart rates, the baseline heart rate was controlled by atrial pacing at 5 to 7 beats above the intrinsic heart rate at rest, and the pacemaker was turned back to this rate after rapid atrial pacing. The cessation of rapid atrial pacing was timed to coincide with the appearance of the intravenous bolus of contrast medium in the left atrium. The intravenous left ventriculogram thus obtained occurred within 4 to 7 beats after pacing.

After the intravenous injection, continuous fluoroscopic images were obtained with a General Electric Fluoricon 300 System (9 inch [22 cm] cesium iodide image intensifier and Plumbicon television camera). These images were acquired using 4.5 to 9.0 mA and 60 to 75 kVp. The analog images were recorded on a high performance video cassette recorder (JVC ¾ inch [1.91 cm] HR 6060Y with a signal to noise ratio of 48 dB) referenced with a modified V5 electrocardiographic signal (Picker cardiac module gating device).

Image generation. After cardiac catheterization, the fluoroscopic analog images recorded on videotape were processed by entry into the memory of a dedicated computer (MDS A^2, Ann Arbor, Michigan) via an analog to digital converter. Before intravenous contrast injection, a single gated cycle of the left ventricle was acquired and referenced by the computer operator as a "mask" and one gated cycle of the left ventricle at peak opacification was acquired into a 128 × 128 matrix at 30 interlaced frames/s with 256 shades of gray. A constant was added to both the contrast and mask images to prevent pixel underflows, the mask image (M) was multiplied by a factor to achieve maximal count densities and the resultant mask image was divided by the contrast image (C) to yield a mask mode image (MM). The formula is represented as follows:

$$MM = \frac{(M + 20) \times 110}{(C + 20)}.$$

A generous region of interest was assigned to the mask mode image, and time versus X-ray transmission curves were generated for each full cardiac cycle. End-diastole was assigned to the image with maximal X-ray attenuation and end-systole to the image with minimal attenuation (1,2,14). Careful endocardial outlines were then drawn for the end-diastolic and end-systolic frames.

The direct left ventriculogram was recorded on 35 mm cine film at 60 frames/s and viewed on a Vanguard cine projector. End-diastolic and end-systolic outlines were drawn by careful visual determination of the largest and smallest endocardial outlines (7).

Wall motion analysis. All direct left ventriculograms were viewed independently by three experienced observers, and the presence or absence of wall motion abnormalities and significant coronary artery lesions was noted. Disagreements were resolved by consensus, and postectopic beats were not used for wall motion analysis (12). Areas were judged to have either normal, hypokinetic, akinetic or dyskinetic wall motion.

Quantitative wall motion analysis was studied independent of the subjective analysis described. A radial shortening method was used for both the direct left ventriculogram and mask mode images. For the direct study, the long axis of the end-diastolic frame was taken from the midpoint of the aortic valve plane to the apex. Because of superimposition

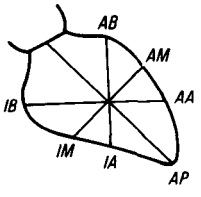
JACC Vol 2, No. 1
July 1983:70–6

of the left atrium, aortic root and basilar areas of the left ventricle during intravenous imaging, the long axis of the mask mode images was considered as the line joining the apex and the center of the area (provided by the computer) of the end-diastolic frame. The potential difference in angles of these long axes was estimated from the direct left ventriculogram by reassigning the axis after drawing a line from the anterior aortic valve plane to the inferior mitral valve plane and then bisecting the ventricle. The difference in the angles of the long axes thus assigned was 10.6 ± 3.3° (13° maximum, 4° minimum).

Percent shortening along seven radii at 45° angles was analyzed (Fig. 1). The radii emanated from the center of area for the mask mode images and the midpoint of the long axis for the direct ventriculograms. A normal range for shortening in each radius was then determined from the values observed in all segments felt to be definitely normal by all three observers. This definition of "normal" was used for several reasons. First, it allowed inclusion of a larger number of radii than would have been provided by our small normal population so that the normal ranges were established from a larger sample size. Second, although the inclusion of normal segments in patients with coronary disease might include some segments with subtle hypokinesia not noted by qualitative inspection, the process might also include equally subtle hypercontractile segments in areas remote from infarcted segments. Thus, to evaluate the usefulness of this quantitation after atrial pacing for assessing functionally important residual ischemic beds (a frequent clinical problem in a referred patient population), we included all segments believed to be qualitatively normal.

Because of the wide range of normal radial shortening (7,10), and in order to maximize the sensitivity, specificity and predictive accuracy of these lower limits for the detection of wall motion abnormalities, we considered the normal lower limit of radial shortening to be 1.5 standard deviations below the mean (10).

Figure 1. The radial shortening method utilized in this study (**left**) is demonstrated together with the normal values observed in each radius and for each technique. DIV = digital intravenous ventriculogram; LVG = direct left ventriculogram.



	NORMAL RADIAL SHORTENING (%)	
	DIV	LVG
ANTEROBASAL (AB)	26 0 ± 6 7	44 8 ± 14 0
ANTEROMEDIAL (AM)	30 7 ± 8 6	46 4 ± 17 6
ANTEROAPICAL (AA)	26 7 ± 7 3	38 2 ± 18 7
APICAL (AP)	28 3 ± 16 8	43 4 ± 23.8
INFEROAPICAL (IA)	36 3 ± 11 3	51 7 ± 18 0
INFEROMEDIAL (IM)	36 0 ± 10 4	50 3 ± 17 6
INFEROBASAL (IB)	19 7 ± 11.8	23 0 ± 8 6

Reproducibility. The radial wall motion was recalculated in 10 patients by one observer on two occasions at least 6 weeks apart and also by a second independent observer.

Statistics. All data are given as mean ± 1 standard deviation. Differences were assessed by the appropriate paired or unpaired Student's *t* test. Correlations were determined by linear regression analysis.

Results

Normal radial shortening. The results of normal radial shortening are shown in Figure 1 for both the digital intravenous ventriculograms and the direct left ventriculograms. The intraobserver variation was ± 8.8% of the percent radial shortening, with an absolute range of difference of −3 to +7% radial shortening units ($y = 0.96x + 1.3$, correlation coefficient [r] = 0.98, probability [p] < 0.001). The interobserver variation was ± 5.3% of the percent radial shortening, with an absolute range of differences of −6 to +6% radial shortening units ($y = 0.96x + 1.3$, $r = 0.99$, $p < 0.001$). On the basis of these results, a significant change in shortening was considered present if radial shortening changed by greater than 7% fractional shortening units (see later).

Comparison of wall motion analyses. With use of 1.5 standard deviations below the mean percent shortening in each radius, the overall agreement in assessing normal or abnormal wall motion between the two techniques was 87% (274 of 315 segments), and disagreements occurred in 13% (41 of 315 segments). The number of disparities per radius was: anterobasal, five; anteromedial, five; anteroapical, seven; apical, eight; inferoapical, five; inferomedial, six and inferobasal, five. These disparaties occurred in areas judged normal or hypokinetic. Both techniques correctly identified all the severe segmental wall motion abnormalities in the 16 patients with prior infarction (two dyskinetic, seven akinetic and seven hypokinetic areas), 10 of whom demonstrated total occlusion of the coronary vessel supplying the abnormal segment.

Agreement between qualitative wall motion assessment and quantitative assessment of the direct left ventriculograms and the digital intravenous ventriculograms was 85% (267 of 315 segments) and 83% (262 of 315 segments), respectively. Again, the disparities occurred only in assessing normal and hypokinetic, not dyskinetic or akinetic, areas.

Correlation of coronary anatomy with wall motion. Abnormalities of radial shortening in the anterobasal, anteromedial or anteroapical segments were considered a result of significant coronary disease of the left anterior descending or diagonal artery and abnormalities of the inferobasal, inferomedial or inferoapical segments were ascribed to significant lesions of the right coronary or circumflex artery systems (15). Abnormalities of the apical segments were

not considered in this analysis unless an adjacent radius also showed abnormal shortening. Thus, 90 perfusion beds were considered in the 45 patients. Fifty-one of those beds were supplied by significantly stenotic coronary vessels but, as expected, quantitative analysis of wall motion at rest revealed abnormalities in only 20 of the 51 beds for the intravenous studies, and 21 beds for the direct ventriculograms (that is, sensitivity of 39 and 41%, respectively, for the detection of significant coronary disease). Furthermore, 16 of these abnormalities could be accounted for by prior infarction, and in 10 of these cases, the segment was supplied by a totally occluded artery. Of the 39 perfusion beds supplied by normal coronary arteries or arteries with subcritical stenoses, 37 and 35, respectively, were associated with normal quantitative wall motion on the digital mask mode (MM) image and direct ventriculogram, (that is, a specificity of 95 and 90%, respectively, for the absence of significant coronary disease).

Effects of atrial pacing. Five normal subjects (4 women and 1 man) and 15 patients with coronary artery disease (12 men and 3 women) underwent a second digital intravenous study after rapid atrial pacing. In the normal group, the control and immediate postpacing heart rates were 78 ± 18 and 73 ± 19 beats/min, respectively (difference not significant [NS]). In the coronary group, the postpacing heart rate was slightly higher than that at rest (76 ± 11 versus 71 ± 11 beats/min, $p < 0.05$), and this was probably due to the induction of ischemia. The peak atrial pacing rates were similar in both groups (140 ± 6 in the normal group and 142 ± 19 in the coronary group, NS).

Although only 6 of the 15 patients with coronary artery disease undergoing rapid atrial pacing demonstrated wall motion abnormalities at rest, all 9 patients with normal wall motion at rest demonstrated significant deterioration in segmental wall motion in the postpacing digital intravenous ventriculogram in areas supplied by significantly narrowed coronary arteries (Fig. 2 and 3). In five of the nine instances, the induced wall motion abnormality demonstrated radial shortening less than the 1.5 standard deviation cut-off, whereas in four cases the deterioration was more subtle, but nevertheless quantifiable as a decrease of greater than 7% radial shortening units. Thus, as expected, the sensitivity for detection of significant coronary disease by quantitative wall motion analysis was increased by pacing-induced ischemia. No wall motion abnormalities were induced in the postpacing digital study in the five patients with normal coronary arteriograms.

The ejection fraction at rest before atrial pacing was normal in all subjects and averaged 77 ± 12% in the normal subjects and 75 ± 10% in the patients with coronary artery

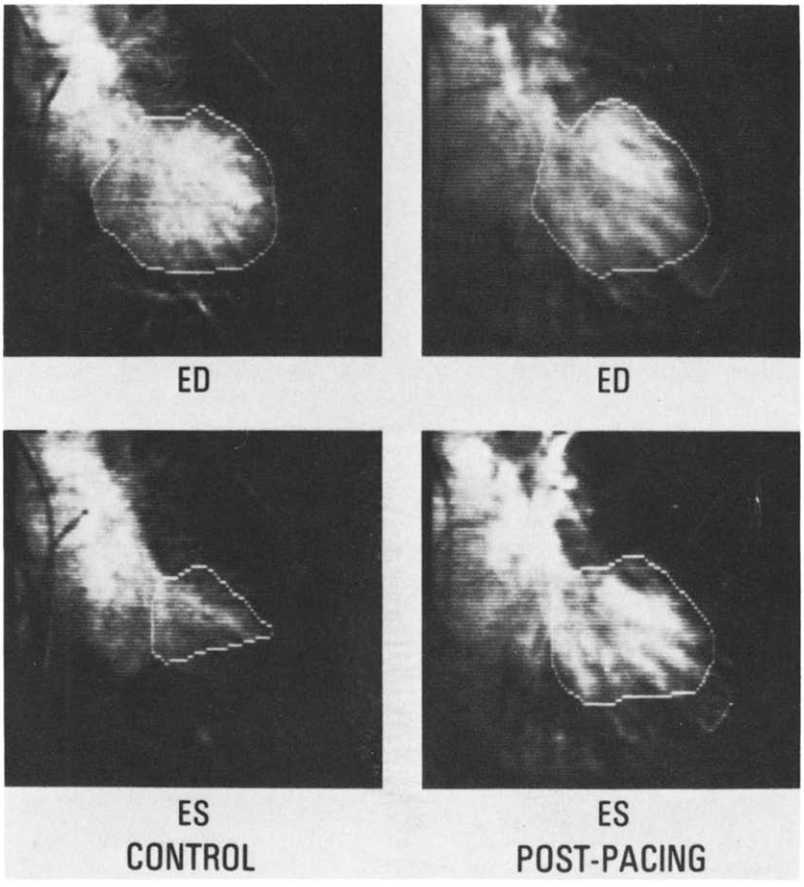


Figure 2. A wall motion abnormality induced by atrial pacing. The mask mode digital intravenous ventriculograms at end-diastole (ED) and end-systole (ES) are shown before and after pacing. In the control state, anterior hypokinesia is present. After pacing, there are deterioration of the anterior wall motion and a new inferior wall motion abnormality.

disease. After pacing, the ejection fraction increased slightly in the normal group (+7 ± 8 units, range +1 to +19) but showed a decrease in the patients (− 10 ± 8 units, range −39 to +5, $p < 0.01$). Eleven (73%) of the 15 patients with coronary artery disease had a decrease in ejection fraction of more than 5 units after atrial pacing.

Discussion

This study establishes that digital intravenous ventriculography can be used for the quantitative study of segmental wall motion and that there is a high degree of agreement between this technique and standard direct left ventriculography when a similar quantitative method is applied to both studies. This high degree of agreement is comparable with preliminary results from other groups using quantitative methods (16) and with results obtained when area methods of wall motion analysis are used (17). Furthermore, deterioration of segmental wall motion in response to an intervention, such as atrial pacing, that induces ischemia can be ascertained and used to increase the sensitivity of wall motion analysis for the detection of significant coronary disease (16).

Discrepancies between intravenous and direct angiographic wall motion studies. There are several reasons for the discrepancies between these two techniques, which occurred in only 13% of radii, and the differences in calculated shortening. First, a drawback of levophase ventricular imaging is the overlap of the left atrium, aortic root and basal portions of the left ventricle which obscures both basal wall motion and the aortic valve plane, the midpoint of which is frequently used as a marker for the long axis of the ventricle. This problem is also inherent in radionuclide studies, requiring the long axis of such images to be defined in a different fashion. In this study, a line through the apex and center of area was used as the long axis of the mask mode images and the radii emanated from the center of area, which was automatically provided by the computer. This reference frame is very similar but not identical to the radial reference frame used in the direct ventriculogram. The differences would be expected to cause discrepancies in assessment of motion in the basilar areas because of overlap and the apical area, which is sensitive to alterations in assignment of the long axis. Indeed, a large number of discrepancies occurred in these radii (18 of 41). Furthermore, because of the difficulties in defining the mitral and aortic valve planes, the computer-generated center of area from the mask mode outlines was generally more apical than the midpoint of the long axis in the direct ventriculograms. This may explain the systematically smaller values for radial shortening obtained from the mask mode images.

True differences in wall motion between the acquisition of the intravenous and direct studies are unlikely because all patients were in a baseline state during these studies and the amount of time between ventriculograms permitted dissipation of the effects of the contrast medium (18). Nevertheless, some persistent lowering of the systemic vascular resistance may have been present during left ventriculography owing to the prior contrast injections; this may also account for the generally larger radial shortening calculations from the direct left ventriculograms. Edge detection from mask mode images and direct ventriculograms is not identical. The image manipulation required may account for this difference (3,19) and, therefore, also for discrepancies in wall motion analysis. The different framing rates of the two acquisitions may also have caused some minor variability in determination of end-diastolic and end-systolic frames. Lastly, we used strict limits for the designation of normal wall motion, and some discrepancies occurred when fractional radial shortening was just above or below these

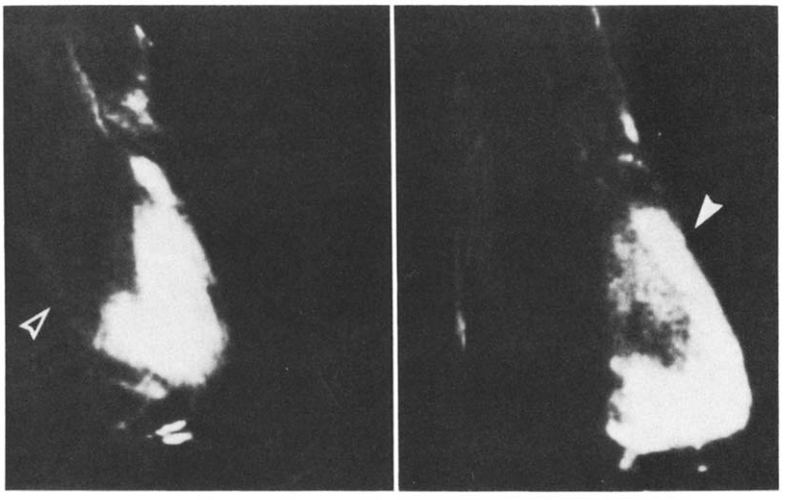


Figure 3. Ejection shell images of a patient with coronary artery disease shown in the control state (**left panel**) and after atrial pacing (**right panel**). The ejection shell is obtained by subtracting the end-systolic frame from the end-diastolic frame leaving an ejection shell that is a single frame summary of wall motion. At rest, normal wall motion in the anterior, apical and inferoapical walls is noted with absence of wall motion in the inferobasal area (evidenced by absence of a white rim, **open arrow**). After atrial pacing, deterioration of anterior wall motion is documented by a thinning of the ejection shell in the anterior wall (**solid arrow**).

limits for the two studies. Nevertheless, the overall agreement approached 90% for both techniques and discrepancies were few.

Role of atrial pacing in wall motion studies. Atrial pacing can induce diagnostic changes in ventricular function in patients with coronary disease (14,20–22). It is well suited to the digital intravenous technique because patient motion, which would be the case for exercise-induced ischemia, is not a problem and registration errors with mask mode imaging of the left ventricle are minimized. Atrial pacing is also particularly useful in patients who cannot exercise to adequate work loads. Furthermore, correlation of ischemic symptoms with wall motion abnormalities would be expected to be useful in patients with electrocardiographic abnormalities at rest that preclude adequate interpretation of stress electrocardiograms (23).

Clinical implications. It is apparent that reliable quantitation of rest and postpacing ventricular function is mandatory before such techniques can be used diagnostically (5). In addition, the quantitative analysis should be simple enough for widespread use without the need for inordinately complex computer facilities. Although the radial shortening method has been shown by some to be relatively insensitive for the detection of wall motion abnormalities (7), no universally acceptable method for wall motion analysis is available and the ability of the radial shortening method to detect clinically relevant changes in wall motion has not been disproved. The results of this study are comparable with preliminary results of other groups using area methods for wall motion analysis (18). Furthermore, this study demonstrates that the present method can detect changes in wall motion that can be correlated with significant coronary stenoses. Indeed, all nine patients with coronary artery disease and normal wall motion at rest who were subjected to atrial pacing showed quantitative deterioration in wall motion as assessed by the radial shortening technique.

It is concluded that digital intravenous ventriculography can be utilized to quantitate left ventricular wall motion with a high degree of agreement with standard direct left ventriculography. Stress-induced wall motion abnormalities can be detected by these quantitative techniques to increase the sensitivity of wall motion analysis for the detection of significant coronary disease. The techniques outlined require only venous cannulation and fluoroscopic X-ray exposure levels. It can conceivably be applied on an outpatient basis, particularly in those patients unable to exercise or with an abnormal rest electrocardiogram that does not permit accurate interpretation during exercise. Despite the known limitations of radial shortening methods for analysis of wall motion at rest (7,10), the technique remains useful for assessing deterioration of wall motion. Furthermore, the high degree of agreement between quantitative assessment of digital intravenous ventriculograms and direct ventriculograms with the simple radial shortening technique used in this study suggests that other methods of wall motion analysis may provide a similarly high degree of agreement.

References

1. Higgins CB, Norris SL, Gerber KH, et al. Quantitation of left ventricular dimensions and function by digital intravenous ventriculography. Radiology 1982;144:461–9.
2. Slutsky RA, Carey P, Higgins CB The effect of acute incremental volume overload on cardiac chamber size, function and the pulmonary circulation: analysis by digital intravenous angiography. Am Heart J 1982,104.254–62.
3. Vas R, Diamond G, Forrester J, Whiting J, Swan HJC. Computer enhancement of direct and venous-injected left ventricular contrast angiography. Am Heart J 1981;102:719–28.
4. Tobis J, Nacioglu O, Johnston W, et al Left ventriculography with digital subtraction angiography using intravenous contrast injection and fluoroscopic exposure levels. Am Heart J 1982;104:20–7.
5. Chaitman BR, De Mots H, Bristow JD, Fosch J, Rahimtoola SH Objective and subjective analysis of left ventricular angiograms. Circulation 1975,52:420–5
6. Smalling R, Cole JS, Skolnik MH Comparison of digital boundary detection and semi-automated analysis of left ventricular cine angiograms. Cathet Cardiovasc Diagn 1979,5.331–46.
7. Gelberg HJ, Brundage BH, Glantz S, Parmley WW. Quantitative left ventricular wall motion analysis: a comparison of area, chord and radial methods Circulation 1979;59.991–1000.
8. Tzivoni D, Diamond G, Pichler M, Stankus K, Vas R, Forrester J Analysis of regional ischemic left ventricular dysfunction by quantitative cineangiography Circulation 1979;60:1278–83
9. Warren SE, Bhargava V, Vieweg WVR, Dennish GW, Alpert JS, Hagan AD Semiautomated method for evaluation of left ventricular regional wall motion in coronary artery disease Am J Cardiol 1980;46.832–6
10. Bhargava V, Warren S, Vieweg WVR, Shabetai R Quantitation of left ventricular wall motion in normal subjects: comparison of various methods. Cathet Cardiovasc Diagn 1980;60:7–16.
11. Doss JK, Hillis LD, Curry G, et al. A new model for the assessment of regional ventricular wall motion Radiology 1982;143:763–70.
12. Dyke SH, Cohn PF, Gorlin R, Sonnenblick EH. Detection of residual myocardial function in coronary artery disease using post-extrasystolic potentiation Circulation 1974;50.694–9.
13. Thadani U, Lewis JR, Mathew TM, West RO, Parker JO. Reproducibility of clinical and hemodynamic parameters during pacing stress testing in patients with angina pectoris Circulation 1970;60:1036–44.
14. Carey P, Slutsky RA, Ashburn W, Higgins CB Validation of cardiac output estimates by digital video subtraction angiography in dogs: correlation with thermodilution estimates. Radiology 1982;143:623–6.
15. Herman MV, Heinle RA, Klein MD, Gorlin R Localized disorders in myocardial contraction. Asynergy and its role in congestive heart failure N Engl J Med 1967:277:222–32.
16. Ross AM, Johnson R, Wasserman AG, et al. Intravenous digital left ventriculography at rest and with atrial pacing as a screening procedure for coronary disease (abstr) Circulation 1982;66(suppl II):II-228.
17. Low R, Nissen S, Booth D, Takeda P, DeMaria A Evaluation of left ventricular function by digital subtraction ventriculography: comparison with cineangiography and interobserver variability (abstr). Circulation 1982;66(suppl II):II-228.
18. Higgins CB, Gerber K, Mattrey R, Slutsky RA. Evaluation of hemodynamic effects of intravenous administration of ionic and nonionic contrast materials: implications for deriving physiologic measurements from CT and digital cardiovascular imaging Radiology 1982;142:681–6

19. Slutsky RA, Mancini GBJ, Ashburn W, Higgins CB. Digital intravenous ventriculography: comparison of volumes from mask-mode and nonsubtracted images with thermodilution and sonocardiometric measurements (abstr). Circulation 1982;66(suppl):II-227.
20. Khaja F, Parker JO, Ledwich RJ, West RO, Armstrong PW. Assessment of ventricular function in coronary artery disease by means of atrial pacing and exercise. Am J Cardiol 1970;26:107–16.
21. Parker JO, Khaja F, Case RB. Analysis of left ventricular function by atrial pacing. Circulation 1971;43:241–52.
22. Pasternac A, Gorlin R, Sonnenblick EH, Kemp HG. Abnormalities of ventricular motion induced by atrial pacing in coronary artery disease. Circulation 1972;45:1195–205.
23. Froelicher VF. Exercise Testing and Training. New York: Le Jacq, 1983:63–6